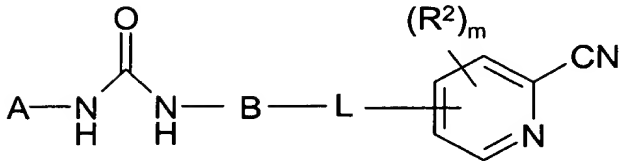
1. A compound of Formula (I)



(I)

or a pharmaceutically acceptable salt, prodrug or metabolite thereof, wherein

A is optionally substituted

pyridinyl,

naphthyl,

8-10 membered bicyclic heteroaryl groups having 1-4 heteroatoms which are O, N, S or combinations thereof,

partially saturated $C_8$-$C_{10}$ bicyclic carbocyclic moieties, bound to the urea moiety through a benzene group, or

partially saturated 8 to 10 membered bicyclic heterocyclic moieties, said heterocyclic moieties having 1-4 heteroatoms which are O, N, S or combinations thereof binding through the benzene or heteroaryl group of the structure,

B is optionally substituted phenyl or naphthyl,

L is O or S,

m is an integer 0,1,2 or 3, and

each $R^2$ is independently selected from

$C_{1-5}$ alkyl,

$C_{1-5}$ haloalkyl,

$C_{1-3}$ alkoxy, N-oxo or N-hydroxy.

2. A compound of claim 1 wherein A of Formula (I) is a partially saturated 8 to 10 membered bicyclic heterocyclic moiety with at least one oxygen atom, and at least one halo-substituent on a saturated carbon atom
of the partially saturated 8 to 10 membered bicyclic heterocyclic moiety.

3. A compound of claim 2 wherein all saturated carbons atoms of the partially saturated 8 to 10 membered bicyclic heterocyclic moiety A of Formula (I) are per-fluorinated.

4. A compound of claim 1, 2 or 3 wherein A is substituted by $(R^3)_n$
wherein n is an integer 0, 1, 2, 3, 4, 5 or 6, and
each $R^3$ is independently

halogen,

$R^4$,

$OR^4$,

$S(O)R^4$,

$C(O)R^4$,

$C(O)NR^4R^5$,

oxo,

cyano or

$NO_2$; and

$R^4$ and $R^5$ are independently

hydrogen,

$C_{1-6}$ alkyl, or

up to per-halogenated $C_{1-6}$ alkyl.

5. A compound of claim 1,2, 3 or 4 wherein B is substituted by $(R^1)_p$ wherein p is an integer 0, 1, 2, 3, or 4,and each $R^1$ is independently

halogen,

$C_{1-5}$ haloalkyl,

$NO_2$;

$C(O)NR^4R^5$,

$C_{1-6}$ alkyl,

$C_{1-6}$ dialkylamine,

$C_{1-3}$ alkylamine,

CN,

amino,

hydroxy or

$C_{1-3}$ alkoxy.

6. A compound of claim 1, 2, 3 or 4 wherein A is optionally substituted pyridinyl.

7. A compound of claim 1, 2, 3 or 4 wherein A is optionally substituted naphthalenyl.

8. A compound of claim 1, 2, 3 or 4 wherein A is optionally substituted 2-, 3-, 4-, 5-, 6-, 7- or 8-quinolinyl, 1-, 3-, 4-, 5-, 6-, 7-, 8- isoquinolinyl, benzimidazol-5-yl, benzimidazol-6-yl, 1,3-benzothiazol-2-yl, 1,3-benzothiazol-5-yl, 1,3-benzothiazol-6-yl, 1,2,3-benzotriazol-5-yl, 1,3-benzoxazol-2-yl, 1,3-benzoxazol-6-yl, 1H-indazol-5-yl, 2H-indazol-5-yl, 1H-indazol-6-yl, 1H-indol-5-ylquinoxalin-2-yl or quinoxalin-6-yl.

9. A compound of claim 1, 2, 3 or 4 wherein A is optionally substituted 2,3-dihydro-1H-indol-5-yl, 2,3-dihydro-1H-indol-6-yl, 2,3-dihydro-1H-inden-4-yl, 2,3-dihydro-1H-inden-5-yl,

10. A compound of claim 1, 2, 3 or 4 wherein A is optionally substituted 1,1-dioxido-2,3-dihydro-1-benzothien-6-yl, , 1-oxo-2,3-dihydro-1H-inden-5-yl, , 2H-benzo[d]1,3-dioxolen-5-yl, 2H-benzo[d]1,3-dioxolen-4-yl, 2,3-dihydrobenzo[b]fur-5-yl, 2H,3H-benzo[e]1,4-dioxan-6-yl, 2H,4H-benzo[e]1,3-dioxan-6-yl, or 2H,4H-benzo[e]1,3-dioxan-8-yl, substituted with at least one halogen.

11. A compound of claim 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 wherein B is phenyl.

12. A compound of claim 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 wherein B is phenyl substituted by at least one halogen.

13. A compound of claim 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 wherein B is phenyl substituted by at least one fluorine atom .

14. A compound of claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 11,12 or 13 wherein L is oxygen.

15. A compound of claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 11,12, 13 or 14 wherein $R^1$ is fluorine, chorine, bromine, methyl, $NO_2$, $C(=O)NH_2$, methoxy, $SCH_3$, trifluoromethyl, or methylsulfonyl.

16. A compound of claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 11,12, 13, 14 or 15 wherein $R^2$ is methyl, ethyl, propyl, oxygen, or cyano.

17. A compound of claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 11,12, 13, 14, 15 or 16, wherein $R^3$ is trifluoromethyl, methyl, ethyl, propyl, butyl, isopropyl, tert-butyl, chlorine, fluorine, bromine, cyano, methoxy, acetyl, trifluoromethyl sulfonyl, trifluoromethoxy, or trifluoromethylthio.

18. A compound which is

{[2-chloro-4-(2-cyano(4-pyridyloxy))phenyl]amino}-N-indan-5-ylcarboxamide;

{[4-(2-cyano(4-pyridyloxy))-2-fluorophenyl]amino}-N-indan-5-ylcarboxamide;

{[2-chloro-4-(2-cyano(4-pyridyloxy))phenyl]amino}-N-(1-oxoindan-5-yl)carboxamide;

{[4-(2-cyano(4-pyridyloxy))-2-fluorophenyl]amino}-N-(2-naphthyl)carboxamide;

N-(2,2-difluorobenzo[d]1,3-dioxolan-5-yl){[4-(2-cyano(4-pyridyloxy))phenyl]amino}carboxamide;

N-(2,2-difluorobenzo[d]1,3-dioxolan-5-yl){[4-(2-cyano(4-pyridyloxy))phenyl]amino}carboxamide;

N-(2,2-difluorobenzo[d]1,3-dioxolan-5-yl){[2-chloro-4-(2-cyano(4-pyridyloxy))phenyl]amino}carboxamide;

N-(2,2-difluorobenzo[d]1,3-dioxolan-5-yl){[3-chloro-4-(2-cyano(4-pyridyloxy))phenyl]amino}carboxamide;

N-(2,2-difluorobenzo[d]1,3-dioxolan-5-yl){[3-chloro-4-(2-cyano(4-pyridyloxy))phenyl]amino}carboxamide;

N-(2,2-difluorobenzo[d]1,3-dioxolan-5-yl){[4-(2-cyano(4-pyridyloxy))-3-fluorophenyl]amino}carboxamide;

{[4-(2-cyano(4-pyridyloxy))-2-(trifluoromethyl)phenyl]amino}-N-(2,2,3,3-tetrafluorobenzo[e]1,4-dioxan-6-yl)carboxamide;

{[2-chloro-4-(2-cyano(4-pyridyloxy))phenyl]amino}-N-(2,2,3,3-tetrafluorobenzo[e]1,4-dioxan-6-yl)carboxamide;

{[4-(2-cyano(4-pyridyloxy))-2-fluorophenyl]amino}-N-(2,2,3,3-tetrafluorobenzo[e]1,4-dioxan-6-yl)carboxamide;

{[4-(2-cyano(4-pyridyloxy))-2,6-difluorophenyl]amino}-N-(2,2,3,3-tetrafluorobenzo[e]1,4-dioxan-6-yl)carboxamide;

{[4-(2-cyano(4-pyridyloxy))-2,5-difluorophenyl]amino}-N-(2,2,3,3-tetrafluorobenzo[e]1,4-dioxan-6-yl)carboxamide;

{[3-chloro-4-(2-cyano(4-pyridyloxy))phenyl]amino}-N-(2,2,3,3-tetrafluorobenzo[e]1,4-dioxan-6-yl)carboxamide;

{[4-(2-cyano(4-pyridyloxy))-2-methylphenyl]amino}-N-(2,2,3,3-tetrafluorobenzo[e]1,4-dioxan-6-yl)carboxamide;

{[4-(2-cyano(4-pyridyloxy))-3-methylphenyl]amino}-N-(2,2,3,3-tetrafluorobenzo[e]1,4-dioxan-6-yl)carboxamide;

{[4-(2-cyano(4-pyridyloxy))-2-nitrophenyl]amino}-N-(2,2,3,3-tetrafluorobenzo[e]1,4-dioxan-6-yl)carboxamide;

{[4-(2-cyano(4-pyridyloxy))phenyl]amino}-N-(2,2,4,4-tetrafluorobenzo[3,4-e]1,3-dioxan-6-yl)carboxamide;

{[4-(2-cyano(4-pyridyloxy))-2-fluorophenyl]amino}-N-(2,2,4,4-tetrafluorobenzo[3,4-e]1,3-dioxan-6-yl)carboxamide;

{[3-chloro-4-(2-cyano(4-pyridyloxy))phenyl]amino}-N-(2,2,4,4-tetrafluorobenzo[3,4-e]1,3-dioxan-6-yl)carboxamide;

{[2-chloro-4-(2-cyano(4-pyridyloxy))phenyl]amino}-N-(2,2,4,4-tetrafluorobenzo[3,4-e]1,3-dioxan-6-yl)carboxamide;

{[4-(2-cyano(4-pyridyloxy))-3-fluorophenyl]amino}-N-(2,2,4,4-tetrafluorobenzo[3,4-e]1,3-dioxan-6-yl)carboxamide;

{[4-(2-cyano(4-pyridyloxy))-2-(trifluoromethyl)phenyl]amino}-N-(2,2,4,4-tetrafluorobenzo[3,4-e]1,3-dioxan-6-yl)carboxamide;

{[4-(2-cyano(4-pyridyloxy))-2,3-difluorophenyl]amino}-N-(2,2,4,4-tetrafluorobenzo[3,4-e]1,3-dioxan-6-yl)carboxamide;

{[4-(2-cyano(4-pyridyloxy))-2,5-difluorophenyl]amino}-N-(2,2,4,4-tetrafluorobenzo[3,4-e]1,3-dioxan-6-yl)carboxamide;

{[4-(2-cyano(4-pyridyloxy))-2,6-difluorophenyl]amino}-N-(2,2,4,4-tetrafluorobenzo[3,4-e]1,3-dioxan-6-yl)carboxamide;

{[4-(2-cyano(4-pyridyl)oxy)-3-methoxyphenyl]amino}-N-(2,2,4,4-tetrafluorobenzo[3,4-e]1,3-dioxan-6-yl)carboxamide;

{[3-bromo-4-(2-cyano(4-pyridyloxy))phenyl]amino}-N-(2,2,4,4-tetrafluorobenzo[3,4-e]1,3-dioxan-6-yl)carboxamide;

{[4-(2-cyano(4-pyridyloxy))-2-methylphenyl]amino}-N-(2,2,4,4-tetrafluorobenzo[3,4-e]1,3-dioxan-6-yl)carboxamide;

{[4-(2-cyano(4-pyridyloxy))-3-methylphenyl]amino}-N-(2,2,4,4-tetrafluorobenzo[3,4-e]1,3-dioxan-6-yl)carboxamide;

5-(2-cyano(4-pyridyl)oxy)-2-{[N-(2,2,4,4-tetrafluorobenzo[3,4-e]1,3-dioxan-6-yl)carbamoyl]amino}benzamide

{[4-(2-cyano(4-pyridyloxy))-2-nitrophenyl]amino}-N-(2,2,4,4-tetrafluorobenzo[3,4-e]1,3-dioxan-6-yl)carboxamide;

{[4-(2-cyano-1-hydroxy(4-pyridyloxy))phenyl]amino}-N-(2,2,4,4-tetrafluorobenzo[3,4-e]1,3-dioxan-6-yl)carboxamide;

{[4-(2-cyano-1-hydroxy(4-pyridyloxy))-2-fluorophenyl]amino}-N-(2,2,4,4-tetrafluorobenzo[3,4-e]1,3-dioxan-6-yl)carboxamide;

{[4-(2-cyano(4-pyridyl)oxy)-2-methylthiophenyl]amino}-N-(2,2,4,4-tetrafluorobenzo[3,4-e]1,3-dioxan-6-yl)carboxamide;

{[4-(2-cyano(4-pyridyl)oxy)-2-(methylsulfonyl)phenyl]amino}-N-(2,2,4,4-tetrafluorobenzo[3,4-e]1,3-dioxan-6-yl)carboxamide;

{[4-(2-cyano(4-pyridyloxy))-2-fluorophenyl]amino}-N-[2-(trifluoromethyl)(4-pyridyl)]carboxamide;

N-[4-(tert-butyl)(2-pyridyl)]{[4-(2-cyano(4-pyridyloxy))phenyl]amino}carboxamide;

N-[4-(tert-butyl)(2-pyridyl)]{[3-chloro-4-(2-cyano(4-pyridyloxy))phenyl]amino}carboxamide;

N-[4-(tert-butyl)(2-pyridyl)]{[4-(2-cyano(4-pyridyloxy))-3-fluorophenyl]amino}carboxamide;

N-[4-(tert-butyl)(2-pyridyl)]{[4-(2-cyano(4-pyridyloxy))-2-fluorophenyl]amino}carboxamide;

N-[4-(tert-butyl)(2-pyridyl)]{[3-bromo-4-(2-cyano(4-pyridyloxy))phenyl]amino}carboxamide;

2-({N-[4-(tert-butyl)(2-pyridyl)]carbamoyl}amino)-5-(2-cyano(4-pyridyl)oxy)benzamide

N-[4-(tert-butyl)(2-pyridyl)]{[4-(2-cyano(4-pyridyloxy))-3-fluorophenyl]amino}carboxamide;

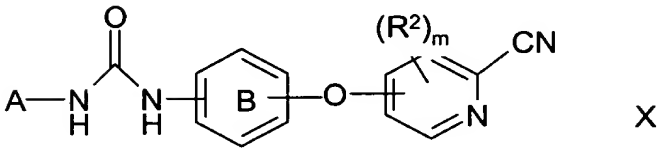
{[4-(2-cyano(4-pyridyloxy))-2-(trifluoromethyl)phenyl]amino}-N-[4-(trifluoromethyl)(2-pyridyl)]carboxamide;

{[4-(2-cyano(4-pyridyloxy))-2,6-difluorophenyl]amino}-N-[4-(trifluoromethyl)(2-pyridyl)]carboxamide;
{[4-(2-cyano(4-pyridyloxy))phenyl]amino}-N-[4-(trifluoromethyl)(2-pyridyl)]carboxamide;
{[4-(2-cyano(4-pyridyloxy))phenyl]amino}-N-(4-ethyl(2-pyridyl))carboxamide;
{[4-(2-cyano(4-pyridyloxy))phenyl]amino}-N-(2-methyl(6-quinolyl))carboxamide;
{[3-chloro-4-(2-cyano(4-pyridyloxy))phenyl]amino}-N-(2-methyl(6-quinolyl))carboxamide;
{[3-chloro-4-(2-cyano(4-pyridyloxy))phenyl]amino}-N-(6-quinolyl)carboxamide;
{[2-chloro-4-(2-cyano(4-pyridyloxy))phenyl]amino}-N-(6-quinolyl)carboxamide;
{[4-(2-cyano(4-pyridyloxy))-2-(trifluoromethyl)phenyl]amino}-N-(6-quinolyl)carboxamide;
{[4-(2-cyano(4-pyridyloxy))phenyl]amino}-N-(3-isoquinolyl)carboxamide;
{[4-(2-cyano(4-pyridyloxy))-2-fluorophenyl]amino}-N-(3-isoquinolyl)carboxamide;
{[3-chloro-4-(2-cyano(4-pyridyloxy))phenyl]amino}-N-(3-isoquinolyl)carboxamide;
{[4-(2-cyano(4-pyridyloxy))phenyl]amino}-N-(1-methyl(1H-indazol-5-yl))carboxamide;
{[4-(2-cyano(4-pyridyloxy))-2-fluorophenyl]amino}-N-(1-methyl(1H-indazol-5-yl))carboxamide;
{[2-chloro-4-(2-cyano(4-pyridyloxy))phenyl]amino}-N-(1-methyl(1H-indazol-5-yl))carboxamide;
{[4-(2-cyano(4-pyridyloxy))-2-(trifluoromethyl)phenyl]amino}-N-(1-methyl(1H-indazol-5-yl))carboxamide;
{[3-chloro-4-(2-cyano(4-pyridyloxy))phenyl]amino}-N-(1-methyl(1H-indazol-5-yl))carboxamide;
{[4-(2-cyano(4-pyridyloxy))phenyl]amino}-N-[2-(trifluoromethyl)benzimidazol-5-yl]carboxamide;
{[3-chloro-4-(2-cyano(4-pyridyloxy))phenyl]amino}-N-[2-(trifluoromethyl)benzimidazol-5-yl]carboxamide;
N-benzothiazol-5-yl{[4-(2-cyano(4-pyridyloxy))-2-nitrophenyl]amino}carboxamide;
{[4-(2-cyano(4-pyridyloxy))-3-methylphenyl]amino}-N-(2-methylbenzothiazol-5-yl)carboxamide; or
salts thereof and stereoisomers thereof.

19. A compound of claim 1, 2 or 3 which is a pharmaceutically acceptable basic salt of an organic acid of formula (I).

20. A compound of claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18, which is a pharmaceutically acceptable acid salt of a compound of formula (I) selected from the group consisting of acid salts of organic and inorganic bases.

21. A compound of Formula X




X

or a pharmaceutically acceptable salt thereof, wherein

A is an optionally substituted
pyridinyl,
naphthyl,

8-10 membered bicyclic heteroaryl groups having 1-4 heteroatoms which are O, N, S or combinations thereof,.

partially saturated $C_8$-$C_{10}$ bicyclic carbocyclic moieties, bound to the urea moiety through a benzene group,

partially saturated 8 to 10 membered bicyclic heterocyclic moieties, said heterocyclic moieties having 1-4 heteroatoms which are O, N, S or combinations thereof,

subject to the proviso that phenyl ring "B" is substituted by at least one fluorine atom,
m is an integer 0, 1, 2 or 3, and

each $R^2$ is independently selected from

$C_{1-5}$ alkyl,

$C_{1-5}$ haloalkyl,

$C_{1-3}$ alkoxy, N-oxo or N-hydroxy.

22. A compound of claim 21 wherein phenyl ring "B" is substituted by 2-4 fluorine atoms.

23. A compound of claim 21 or 22 wherein A is substituted by $(R^3)_n$ and wherein
n is an integer 0, 1, 2, 3, 4, 5 or 6, and
each $R^3$ is independently selected from

halogen ,

$R^4$,

$OR^4$,

$S(O)R^4$,

$C(O)R^4$,

$C(O)NR^4R^5$,

oxo,

cyano or

$NO_2$; and

$R^4$ and $R^5$ are independently

hydrogen,

$C_{1-6}$ alkyl, or

up to per-halogenated $C_{1-6}$ alkyl.

24. A compound of claim 21, 22 or 23 wherein A is optionally substituted pyridinyl.

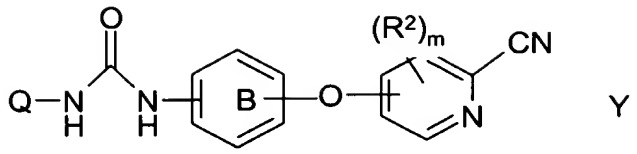
25. A compound of claim 21, 22 or 23 wherein A is optionally substituted naphthalenyl.

26. A compound of claim 21, 22 or 23 wherein A is optionally substituted 2-, 3-, 4-, 5-, 6-, 7- or 8-quinolinyl, 1-, 3-, 4-, 5-, 6-, 7-, 8- isoquinolinyl, benzimidazol-5-yl, benzimidazol-6-yl, 1,3-benzothiazol-2-yl, 1,3-benzothiazol-5-yl, 1,3-benzothiazol-6-yl, 1,2,3-benzotriazol-5-yl, 1,3-benzoxazol-2-yl, 1,3-benzoxazol-6-yl, 1H-indazol-5-yl, 2H-indazol-5-yl, 1H-indazol-6-yl, 1H-indol-5-ylquinoxalin-2-yl or quinoxalin-6-yl.

27. A compound of claim 21, 22 or 23 wherein A is 2,3-dihydro-1H-indol-5-yl, 2,3-dihydro-1H-indol-6-yl, 2,3-dihydro-1H-inden-4-yl, 2,3-dihydro-1H-inden-5-yl,

28. A compound of claim 21, 22 or 23 wherein A is 1,1-dioxido-2,3-dihydro-1-benzothien-6-yl, , 1-oxo-2,3-dihydro-1H-inden-5-yl, , 2H-benzo[d]1,3-dioxolen-5-yl, 2H-benzo[d]1,3-dioxolen-4-yl, 2,3-dihydrobenzo[b]fur-5-yl, 2H,3H-benzo[e]1,4-dioxan-6-yl, 2H,4H-benzo[e]1,3-dioxan-6-yl, or 2H,4H-benzo[e]1,3-dioxan-8-yl, substituted with at least one halogen.

29. A compound of Formula Y



Y

or a pharmaceutically acceptable salt thereof, wherein

Q is a partially saturated 8 to 10 membered bicyclic heterocyclic moiety having 1-4 heteroatoms which are O, N, S or combinations thereof, which is substituted by at least one fluorine atom,
m is an integer 0, 1, 2 or 3, and

each $R^2$ is independently selected from

$C_{1-5}$ alkyl,

$C_{1-5}$ haloalkyl,

$C_{1-3}$ alkoxy, N-oxo or N-hydroxy;

subject to the proviso that phenyl ring "B" is substituted by at least one fluorine atom.

30. A compound of claim 29 wherein phenyl ring "B" is substituted by 2-4 fluorine atoms and Q is substituted by 2-4 fluorine atoms.

31). A compound of claim 29 or 30 wherein A is substituted by $(R^3\text{-})_n$ and wherein n is an integer 0, 1, 2, 3, 4, 5 or 6, and
each $R^3$ is independently selected from

halogen ,

$R^4$,

$OR^4$,

$S(O)R^4$,

$C(O)R^4$,

$C(O)NR^4R^5$,

oxo,

cyano or

nitro ($NO_2$); and

$R^4$ and $R^5$ are independently selected from

hydrogen,

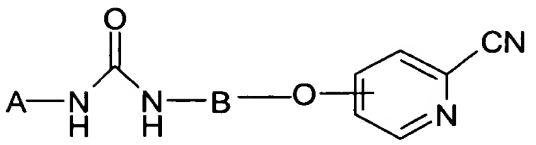
$C_{1-6}$ alkyl,

up to per-halogenated $C_{1-6}$ alkyl.

32. A compound of claim 29 or 30, wherein A is 2,3-dihydro-1H-indol-5-yl, 2,3-dihydro-1H-indol-6-yl, 2,3-dihydro-1H-inden-4-yl, 2,3-dihydro-1H-inden-5-yl, 1,1-dioxido-2,3-dihydro-1-benzothien-6-yl, , 1-oxo-2,3-dihydro-1H-inden-5-yl, , 2H-benzo[d]1,3-dioxolen-5-yl, 2H-benzo[d]1,3-dioxolen-4-yl, 2,3-dihydrobenzo[b]fur-5-yl, 2H,3H-benzo[e]1,4-dioxan-6-yl, 2H,4H-benzo[e]1,3-dioxan-6-yl, or 2H,4H-benzo[e]1,3-dioxan-8-yl, substituted with at least one halogen.

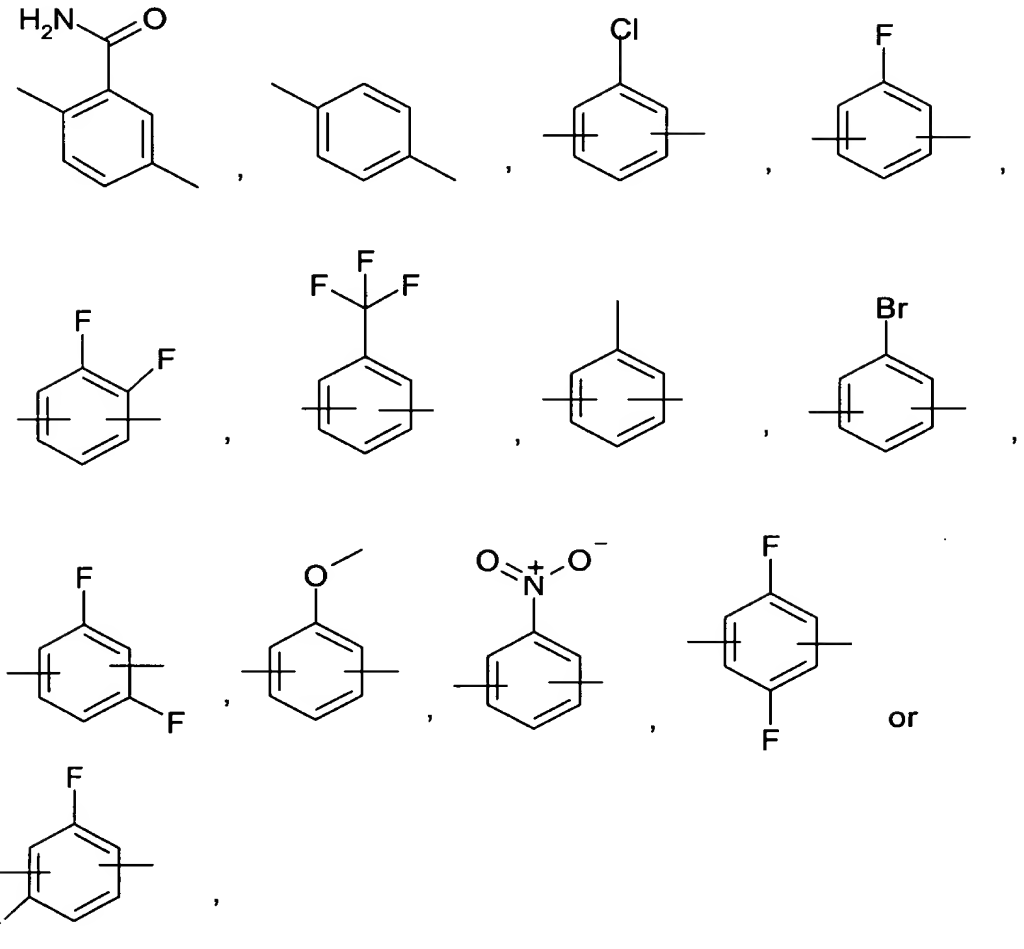
33. A compound of claim 29 or 30 wherein A is
2,2,4,4-tetrafluorobenzo[3,4-e]1,3-dioxan-6-yl,
2,2,3,3-tetrafluorobenzo[e]1,4-dioxan-6-yl or
2,2-difluorobenzo[d]1,3-dioxolan-5-yl.

34. A compound of formula II below



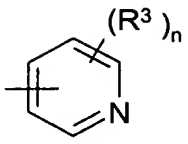
II

wherein B of formula II is



wherein the urea group, –NH-C(O)-NH-, and the bridging group, L, are not bound to contiguous ring carbons of B, but rather have 1 or 2 ring carbons separating them,

A of formula (II) is



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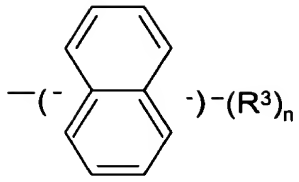

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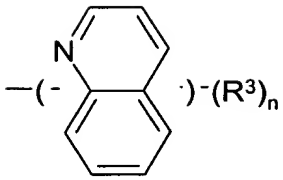

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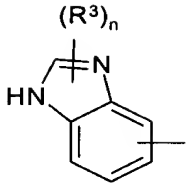

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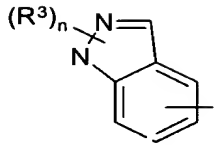

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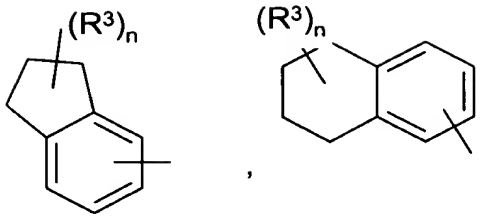
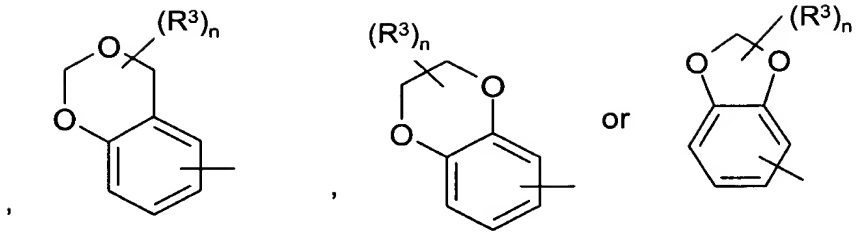


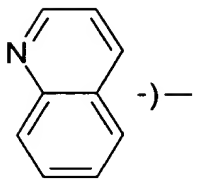




wherein the variable n is 0, 1, 2, 3 or 4,

and $R^3$ is trifluoromethyl, methyl, ethyl, propyl, butyl, isopropyl, tert-butyl, chlorine, fluorine, bromine, cyano, methoxy, acetyl, trifluoromethanesulfonyl, trifluoromethoxy, or trifluoromethylthio.

35. A compound of claim 34 wherein each $R^3$ substituent is fluorine.

36. A compound of claim 34 wherein A of formula II is



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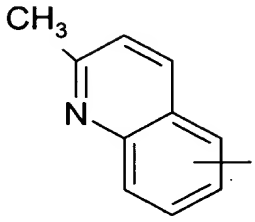

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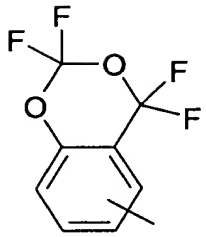

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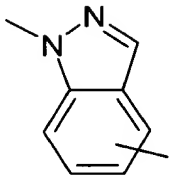

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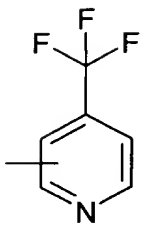

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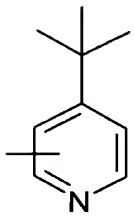

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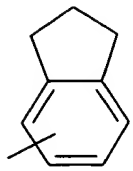
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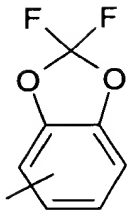

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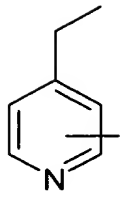

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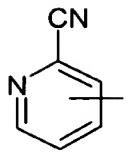

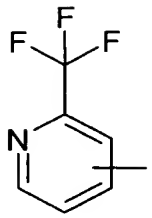


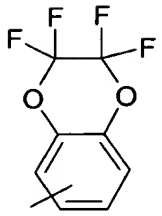

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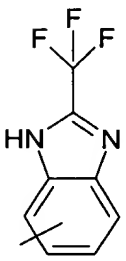

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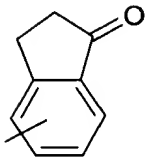

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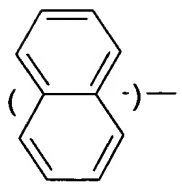

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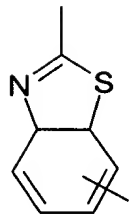

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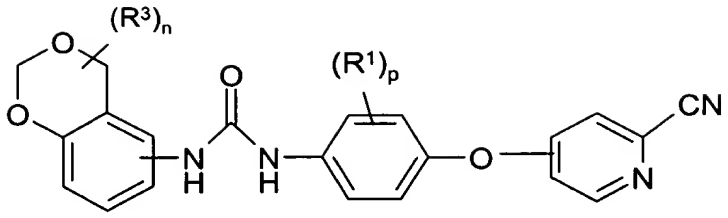
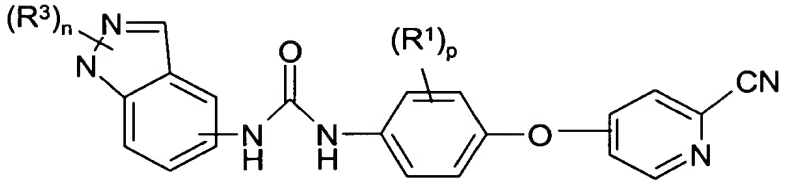
and B of formula II is phenylene, fluoro substituted phenylene or difluoro substituted phenylene.

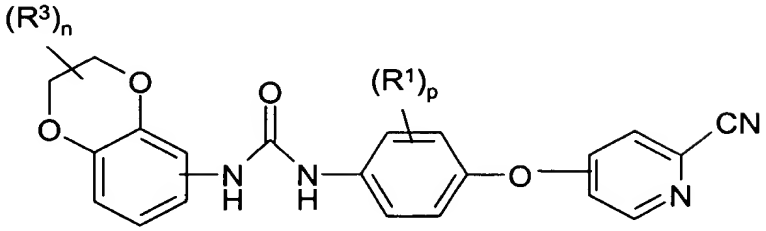
37. A compound of formulae Za, Zb, Zc or Zd:



Za

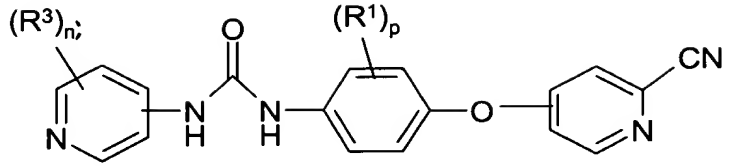


Zb



Zc

and



Zd

or a pharmaceutically acceptable salt, prodrug or metabolite thereof,

wherein

each $R^1$ is independently halogen or trifluoromethyl and

each $R^3$ is independently halogen, $R^4$, $OR^4$, $S(O)R^4$,$C(O)R^4$, $C(O)NR^4R^5$, oxo or cyano ornitro ($NO_2$),

the variable n is 0, 1, 2, 3 or 4 and

the variable p is 0 , 1 or 2.

38. A compound as in claim 37 wherein $R^3$ and is fluoro, trifluoromethyl, methyl or t-butyl.

39. A pharmaceutical composition comprising a compound of claim 1, 2 or 3 or a pharmaceutically acceptable salt thereof, and a physiologically acceptable carrier.

40. A method of treating hyper-proliferative disorders comprising administering to a mammal in need thereof a therapeutically effective amount of a compound of claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 , 18, 20, 34 or 37, or a pharmaceutically acceptable salt or ester thereof.

41. A method according to claim 40, wherein said hyper-proliferative disorder is cancer.

42. A method according to claim 40 or 41, wherein said cancer is of the breast, respiratory tract, brain, reproductive organs, digestive tract, urinary tract, eye, liver, skin, head and/or neck, thyroid, parathyroid and/or their distant metastases.

43. A method according to claim 40 or 41, wherein said cancer is lymphoma, sarcoma, or leukemia.

44. A method according to claim 42, wherein said breast cancer is invasive ductal carcinoma, invasive lobular carcinoma, ductal carcinoma in situ, or lobular carcinoma in situ.

45. A method according to claim 42, wherein said respiratory tract cancer is small-cell lung carcinoma, non-small-cell lung carcinoma, bronchial adenoma or pleuropulmonary blastoma.

46. A method according to claim 42, wherein said brain cancer is a tumor of the brain stem, hypophtalmic glioma, cerebellar astrocytoma, cerebral astrocytoma, medulloblastoma, ependymoma, neuroectodermal or pineal tumor.

47. A method according to claim 42, wherein said tumor of the male reproductive organ is a prostate or testicular cancer.

48. A method according to claim 42, wherein said cancer of the female reproductive organ is endometrial, cervical, ovarian, vaginal, vulvar, or sarcoma of the uterus.

49. A method according to claim 42, wherein said cancer of the digestive tract is anal, colon, colorectal, esophageal, gallbladder, gastric, pancreatic, rectal, small-intestine, orsalivary gland.

50. A method according to claim 42, wherein said cancer of the urinary tract is bladder, penile, kidney, renal pelvis, ureter or urethral.

51. A method according to claim 42, wherein said eye cancer is intraocular melanoma or retinoblastoma.

52. A method according to claim 42, wherein said liver cancer is hepatocellular carcinoma, liver cell carcinomas with or without fibrolamellar variant, cholangiocarcinoma or mixed hepatocellular cholangiocarcinoma.

53. A method according to claim 42, wherein said skin cancer is squamous cell carcinoma, Kaposi's sarcoma, malignant melanoma, Merkel cell skin cancer or non-melanoma skin cancer.

54. A method according to claim 42, wherein said head-and-neck cancer is laryngeal, hypopharyngeal , nasopharyngeal , oropharyngeal, lip or oral cavity cancer.

55. A method according to claim 42, wherein said lymphoma is AIDS-related lymphoma, non-Hodgkin's lymphoma, cutaneous T-cell lymphoma, Hodgkin's disease or lymphoma of the central nervous system.

56. A method according to claim 42, wherein said sarcomas is a sarcoma of the soft tissue, osteosarcoma, malignant fibrous histiocytoma, lymphosarcoma or rhabdomyosarcoma.

57. A method according to claim 42, wherein said leukemia is acute myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia or hairy cell leukemia.

58. A method of treating angiogenesis disorders comprising administering to a mammal in need thereof a therapeutically effective amount of a compound of claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18, or a pharmaceutically acceptable salt or ester thereof.

59. A composition of claim 39, further including an additional pharmaceutical agent.

60. A composition of claim 39, further including an additional anti-cancer agent.

61. A composition of claim 39, further including an anti-hyper-proliferative agent.

62. A composition of claim 61, wherein said anti-hyper-proliferative agent is epothiline or its derivative, irinotecan, raloxifen or topotecan.

62. A composition of claim 59, wherein said additional pharmaceutical agent is aldesleukin, alendronic acid, alfaferone, alitretinoin, allopurinol, aloprim, aloxi, altretamine, aminoglutethimide, amifostine, amrubicin, amsacrine, anastrozole, anzmet, aranesp, arglabin, arsenic trioxide, aromasin, 5-azacytidine, azathioprine, BCG or tice BCG, bestatin, betamethasone acetate, betamethasone sodium phosphate, bexarotene, bleomycin sulfate, broxuridine , bortezomib, busulfan, calcitonin, campath, capecitabine, carboplatin, casodex, cefesone, celmoleukin, cerubidine, chlorambucil, cisplatin, cladribine, cladribine, clodronic acid, cyclophosphamide, cytarabine, dacarbazine, dactinomycin, DaunoXome, decadron, decadron phosphate, delestrogen, denileukin diftitox, depo-medrol, deslorelin, dexrazoxane, diethylstilbestrol, diflucan, docetaxel, doxifluridine, doxorubicin, dronabinol, DW-166HC, eligard, elitek, ellence, emend, epirubicin, epoetin alfa, epogen, eptaplatin, ergamisol, estrace, estradiol, estramustine phosphate sodium, ethinyl estradiol, ethyol, etidronic acid, etopophos, etoposide, fadrozole, farston, filgrastim, finasteride, fligrastim, floxuridine, fluconazole,

fludarabine, 5-fluorodeoxyuridine monophosphate, 5-fluorouracil (5-FU), fluoxymesterone, flutamide, formestane, fosteabine, fotemustine, fulvestrant, gammagard, gemcitabine, gemtuzumab, gleevec, gliadel, goserelin, granisetron HCl, histrelin, hycamtin, hydrocortone, eyrthro-hydroxynonyladenine, hydroxyurea, ibritumomab tiuxetan, idarubicin, ifosfamide, interferon alpha, interferon-alpha 2, interferon alfa-2A, interferon alfa-2B, interferon alfa-n1, interferon alfa-n3, interferon beta, interferon gamma-1a, interleukin-2, intron A, iressa, irinotecan, kytril, lentinan sulphate, letrozole, leucovorin, leuprolide, leuprolide acetate, levamisole, levofolinic acid calcium salt, levothroid, levoxyl, lomustine, lonidamine, marinol, mechlorethamine, mecobalamin, medroxyprogesterone acetate, megestrol acetate, melphalan, menest, 6-mercaptopurine, Mesna, methotrexate, metvix, miltefosine, minocycline, mitomycin C, mitotane, mitoxantrone, Modrenal, Myocet, nedaplatin, neulasta, neumega, neupogen, nilutamide, nolvadex, NSC-631570, OCT-43, octreotide, ondansetron HCl, orapred, oxaliplatin, paclitaxel, pediapred, pegaspargase, Pegasys, pentostatin, picibanil, pilocarpine HCl, pirarubicin, plicamycin, porfimer sodium, prednimustine, prednisolone, prednisone, premarin, procarbazine, procrit, raltitrexed, rebif, rhenium-186 etidronate, rituximab, roferon-A, romurtide, salagen, sandostatin, sargramostim, semustine, sizofiran, sobuzoxane, solu-medrol, sparfosic acid, stem-cell therapy, streptozocin, strontium-89 chloride, synthroid, tamoxifen, tamsulosin, tasonermin, tastolactone, taxotere, teceleukin, temozolomide, teniposide, testosterone propionate, testred, thioguanine, thiotepa, thyrotropin, tiludronic acid, topotecan, toremifene, tositumomab, trastuzumab, treosulfan, tretinoin, trexall, trimethylmelamine, trimetrexate, triptorelin acetate, triptorelin pamoate, UFT, uridine, valrubicin, vesnarinone, vinblastine, vincristine, vindesine, vinorelbine, virulizin, zinecard, zinostatin stimalamer, zofran,

ABI-007, acolbifene, actimmune, affinitak, aminopterin, arzoxifene, asoprisnil, atamestane, atrasentan, BAY 43-9006, avastin, CCI-779, CDC-501, celebrex, cetuximab, crisnatol, cyproterone acetate, decitabine, DN-101, doxorubicin-MTC, dSLIM, dutasteride, edotecarin, eflornithine, exatecan, fenretinide, histamine dihydrochloride, histrelin hydrogel implant, holmium-166 DOTMP, ibandronic acid, interferon gamma, intron-PEG, ixabepilone, keyhole limpet hemocyanin, L-651582, lanreotide, lasofoxifene, libra, lonafarnib, miproxifene, minodronate, MS-209, liposomal MTP-PE, MX-6, nafarelin, nemorubicin, neovastat, nolatrexed,

oblimersen, onco-TCS, osidem, paclitaxel polyglutamate, pamidronate disodium, PN-401, QS-21, quazepam, R-1549, raloxifene, ranpirnase, 13-cis -retinoic acid, satraplatin, seocalcitol, T-138067, tarceva, taxoprexin, thymosin alpha 1, tiazofurine, tipifarnib, tirapazamine, TLK-286, toremifene, TransMID-107R, valspodar, vapreotide, vatalanib, verteporfin, vinflunine, Z-100, zoledronic acid or combinations thereof.